CLAIMS

What is claimed is:

1. A method of manipulating a solid, which comprises:

(a) providing a bed of powder of known weight and uniform height;

(b) inserting a tube a controlled distance into the bed to obtain a plug of powder, wherein the tube has an interior that accommodates a means of ejecting materials from within the tube;

(c) removing the tube from the bed; and

(d) ejecting the plug of powder.

2. The method of claim 1, wherein:

(a) the tube is inserted completely through the bed;

(b) the plug of powder is obtained by compression;

(c) the means of ejecting the plug is a piston, vibration, pressurized gas, or a liquid;

(d) the means of ejecting the plug of (c) is a piston;

(e) the method does not substantially affect the form of the solid; or

(f) the powder comprises an active pharmaceutical ingredient.

3. A method for dispensing a controlled mass of a solid, which comprises:

(a) processing the solid into a powder with an average particle size of less than about 200 micrometers;

(b) forming a powder bed with a predetermined mass and uniform height from a portion of the powder;

(c) inserting a tube a controlled distance into the powder bed to obtain a plug of powder, wherein the tube has an interior that accommodates a means for ejecting materials from within the tube;

(d) lifting the tube from the powder bed;

(e) moving the tube over a target location; and

(f) ejecting a plug of powder onto target location.

4. The method of claim 3, wherein:

(a) the method further comprises:

(i) providing a grille plate with an array of holes sized so that the tube can pass through each with a small clearance; and

(ii) holding the grille plate on top of the powder bed;

the powder bed is prevented from breaking apart upon insertion of the tube;

(c) a method to form the powder bed comprises:

(i) providing a source receptacle assembly comprising:

(1) a source receptacle with sides, a top surface, a bottom face, and at least one cylindrical hole that passes through and is perpendicular to the bottom face; and

(2) a base plate that is removeably attached to the bottom face;

(ii) dispensing a predetermined mass of the powder into the cylindrical hole;

(iii) providing a cylindrical pin with at least one flat, perpendicular end face;

(iv) inserting the cylindrical pin into the cylindrical hole and pressing the pin into the powder with a predetermined force;

(v) rotating the cylindrical pin through an angle of at least 1 degree of rotation with the predetermined force applied; and simultaneously rotating and lifting the pin out of the cylindrical hole;

(d) a method is used for forming the powder bed comprising the steps of:

(i) providing a source receptacle assembly comprising:

(1) a source receptacle with sides, a top face, a bottom surface, and at least one cylindrical hole that passes through and is perpendicular to the top face;

(2) a close fitting cylinder disposed inside of the cylindrical hole; and

(3) a cylinder locking means which allows the close fitting cylinder to be either locked to or disengaged from the source receptacle;

(ii) dispensing a predetermined mass of the powder into the cylindrical hole through the top face of the source receptacle;

(iii) providing a slide plate with at least one flat face;

(iv) pressing the flat face of the slide plate against the top face of the source receptacle;

(v) disengaging the cylinder locking means;

(vi) pressing the cylinder into the powder with a predetermined force;

(vii) rotating the cylinder through an angle of at least 1 degree of rotation with the predetermined force applied;

(viii) engaging the cylinder locking means; and

sliding the slide plate off of the top face of the source receptacle;

(e) pressures applied to the powder are low enough so as to not substantially affect the form of the powder;

(f) the powder comprises an active pharmaceutical ingredient;

(g) the ejecting means is a close fitting pin disposed in the interior of the tube;

(h) the plug inside the tube is compressed prior to being ejected;

(i) the tube is inserted completely through the powder bed;

(j) the ejecting means is a close fitting pin with sides and a face disposed in the interior of the tube, and the close fitting pin is held stationary relative to the tube while the tube is inserted into the powder bed a predetermined depth sufficient to make the pin face contact the powder;

(k) the tube is inserted into the powder with a predetermined force applied to it;

(l) the tube is inserted into the powder bed a predetermined depth;

(m) the tube is a hollow needle; or

(n) a wide variety of solids can be dispensed in controlled amounts without substantially affecting their form.

5. An apparatus for manipulating a solid, which comprises:

(a) a punching assembly comprising a tube having an interior, a piston located within the interior of the tube, a first actuator capable of adjusting the vertical position of the tube, and a second actuator capable of moving the piston within the tube;

(b) a powder bed assembly mounted below the punching assembly, comprising a source plate and a receiving plate; and

(c) a means of positioning the punching assembly over the source plate and the receiving plate.

6. An apparatus for dispensing powder which comprises:

(a) a punching assembly comprising a tube having an interior, close fitting pin disposed inside the interior of the tube, a first actuator capable of adjusting the vertical position of the tube, a second actuator capable of moving the pin within the tube;

(b) a source station comprising at least one powder bed of predetermined mass and uniform height, and a structure to support the powder bed;

(c) a receiving plate mounted below the punching assembly; and

(d) a means for positioning the punching assembly over the source plate and the receiving plate.

7. The apparatus of claim 6, wherein:

(a) the first actuator and the second actuator are pneumatically driven linear actuators;

(b) the first actuator and the second actuator are electronically driven linear servos;

(c) the means for positioning the punching assembly comprises perpendicularly mounted electronically driven linear servos;

(d) a wash station is included which contains means for washing away powder from the tube and the pin, and drying the hollow needle and the pin;

(e) a weigh station is included which contains means for weighing powder that is dispensed into it;

(f) the tube is a hollow needle; or

(g) a wide variety of solids can be dispensed in controlled amounts without substantially affecting their form.

8. A method of manipulating a solid, which comprises:

(a) blending a controlled amount of the solid with a liquid to provide a slurry;

(b) dispensing a controlled amount of the slurry; and

(c) removing the liquid to provide an amount of the solid, wherein the amount of the solid is less than about 1 mg.

9. The method of claim 8, wherein:

(a) the amount of solid is less than about 0.5 mg;

(b) the amount of solid is less that about 100 micrograms;

(c) the means of removing the liquid is evaporation, filtration, or sedimentation;

(d) the solid comprises an active pharmaceutical ingredient;

(d) the solid comprises an active pharmaceutical ingredient;

(e) the method does not substantially affect the form of the solid;

(f) the liquid comprises a wetting agent and water;

(g) the wetting agent is isopropyl alcohol, methanol, PVP, Tween®, or sodium lauryl sulfate; or

(h) solid state analysis is performed after removing the liquid to verify that the solid has not changed form.

10. A method of manipulating a solid, which comprises:

contacting particles of the solid with a surface comprising a plurality of discrete adhesive areas separated by non-adhesive areas, wherein the size of the adhesive areas is smaller than about 5 cm^2, under conditions sufficient to adhere the particles non-electrostatically to an adhesive area; and

adhering the particles non-electrostatically to the adhesive area.

11. The method of claim 10, wherein:

less than about 1 mg of solid is adhered to an adhesive area;

less than about 0.5 mg of solid is adhered to an adhesive area;

(c) less than about 0.25 mg of solid is adhered to an adhesive area;

(d) the adhesive material is a pressure sensitive adhesive, a silicone, or a hydrogel;

(e) the solid comprises an active pharmaceutical ingredient; or

(f) the method does not substantially affect the form of the solid.

12. An apparatus for manipulating a solid, which comprises:

(a) a surface, comprising a plurality of discrete adhesive areas separated by non-adhesive areas, wherein the size of the adhesive areas is smaller than about 5 cm^2, under conditions sufficient to adhere the particles non-electrostatically to an adhesive area at least a portion of which is coated with an adhesive;

(b) a container capable of holding powder; and

(c) a means of contacting the adhesive portion of the surface with powder in the container.

13. The apparatus of claim 12, wherein the adhesive material is a pressure sensitive adhesive, a silicone, or a hydrogel.

14. A method for manipulating a solid, which comprises:
dispensing a known amount of solid into a source chamber;
compressing the solid;
moving a slide plate such that a dose chamber traverses the solid;
moving the dose chamber over a target well; and
ejecting a plug of solid.

15. The method for manipulating a solid of claim 14, wherein

(a) the slide plate in step (c) is moved in a criss-cross or in a spiral trajectory; or

(b) the source chamber is subjected to vibration or mixing in step (c).

16. An apparatus for manipulating a solid, which comprises:

a slide plate comprising a dose chamber;

a powder bed assembly mounted below the slide plate, comprising a source chamber and a receiving plate; and

a means for positioning the slide plate over the source plate and the receiving plate.

17. The apparatus for manipulating a solid of claim 16, wherein:

the apparatus further comprises a microbalance; or

the slide plate comprises a dose chamber in the form of a grid cutter.

18. A method of manipulating a solid, which comprises:

dispensing a known amount of solid into a source chamber;

compressing the solid;

moving a slide plate directly below the source chamber;

pressing the solid through a grid cutter to make multiple plugs;

moving the slide plate to an ejector pin; and

propelling ejector pin down to eject a solid plug into a target well.

19. The method of claim 18, wherein:

the height of each partition in the grid cutter is controlled by a micrometer;

the target well is controlled by an x servo and a y servo; or

the target well is controlled by an x linear actuator and a y linear actuator.

20. A method of transferring a solid, which comprises:

gripping a vessel containing a solid with a clamp;

attaching a swing arm to the clamp;

accelerating the swing arm through an arc trajectory until a hard stop is impacted; and

placing a target well directly below the stopped position of the vessel.

21. The method of claim 20, wherein:

a carousel enables simultaneous transferring and weighing;

the target well is controlled by an x servo and a y servo;

the target well is controlled by an x linear actuator and a y linear actuator;
solid transfer is promoted by a vibrating actuator; or
premature solid transfer is prevented by a retractable shield.

22. An apparatus for transferring a solid, which comprises:
a vessel containing a solid gripped by a clamp;
a swing arm attached to the clamp;
a hard stop;
a target well; and
an x actuator and a y actuator to control the position of the target well.

23. The apparatus of claim 22, wherein:
the actuators are linear servos;
the apparatus further comprises a carousel;
the apparatus further comprises a vibrating actuator;
the apparatus further comprises a retractable shield;
the target vessel is a multi-well plate; or
the apparatus further comprises a microbalance.

24. A method of transferring a solid, which comprises:
gripping a vessel with a mechanical device mounted to xy linear actuators; and
moving the vessel between a receiving plate and a microbalance using the mechanical device mounted to the xy linear actuators.

25. An apparatus for transferring a solid, which comprises:
a vessel gripped by a mechanical device;
the mechanical device is mounted to xy linear actuators;
a receiving plate; and
a microbalance.

26. A method for mixing small amounts of solids, which comprises:
placing the solid in a filter-bottom well;
sealing the well; and

injecting gas into the well.

27. The method of claim 26, wherein:
the well is sealed with a filter plate;
the well is sealed with a lid; or
the seal is pierceable.

28. An apparatus for mixing small amounts of solids, which comprises:
a well with a filter bottom containing solids;
a seal; and
a means for injecting gas into the well.

29. A method to weigh a small amount of solid, which comprises:
supporting a low-mass container with a cradle;
positioning the cradle so the low-mass container is above a weigh platform;
lowering the cradle so the low-mass container is supported by the weigh platform; and
weighing the solid.

30. An apparatus to weigh a small amount of solid, which comprises:
a low mass container containing solid and supported by a cradle;
a weigh platform; and
means for lowering the cradle so the low-mass container is supported by the weigh platform.

31. The apparatus of claim 30, further comprising:
xy linear actuators; or
a two-dimensional array of low-mass containers.

32. A method for measuring the mass of a small amount of solid, which comprises:
coring a plug of powder with a coring tube;
generating a voltage signal;

applying the voltage signal to a piezoelectric actuator affixed to the coring tube; and

measuring the displacement of the coring tube with a laser.

33. The method of claim 32, wherein:

the voltage signal is a swept-sine signal; or

the frequency of the applied voltage signal is between 6.3 kHz and 7.1 kHz.

34. An apparatus for measuring the mass of a small amount of solid, which comprises:

a coring tube;

a function generator;

a piezoelectric actuator affixed to the coring tube,

a laser aligned with the coring tube.

35. A method for measuring the mass of a small amount of solid, which comprises:

attracting dielectric particles to an electrode by imposing a non-uniform electric field;

generating a voltage signal;

applying the voltage signal to a piezoelectric actuator affixed to the electrode; and

measuring the displacement of the electrode with a laser.

36. The method of claim 35, wherein:

(a) the voltage signal is a swept-sine signal; or

(b) the frequency of the applied voltage signal is between 3.6 kHz and 4.0 kHz.

37. An apparatus for measuring the mass of a small amount of solid, which comprises:

an electrode;

a function generator;

a piezoelectric actuator affixed to the electrode; and

a laser aligned with the electrode.